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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/921,045	08/02/2001	David Dorris	10907/20	7635

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EXAMINER	
LY, CHEYNE D	

ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 06/14/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/921,045	DORRIS ET AL.	
	Examiner	Art Unit	
	Cheyne D Ly	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 March 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-67* is/are pending in the application.

4a) Of the above claim(s) *4,6-15,19,21,22 and 51-67* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3, 5, 16-18, 20, and 23-50* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-67* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicants' arguments filed March 29, 2004 have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

2. Claims 1-3, 5, 16-18, 20, and 23-50 are examined on the merits.

3. FINAL OFFICE ACTION.

CLAIM REJECTIONS - 35 U.S.C. § 112, SECOND PARAGRAPH

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 17, 18, 20, and 23-28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

6. This rejection is maintained with respect to claims 17, 18, 20, and 23-28, as recited in the previous office action mailed December 29, 2003.

RESPONSE TO ARGUMENT

7. Applicant's argument, via pointed to disclosure (page 4, lines 4-11) that said disclosure in the instant specification is clear to one skilled in the art in regard to the limitation of "complementary" in the elected claims, has been fully considered and found to be unpersuasive as discussed below. The pointed to support discloses "a target nucleic acid of complementary sequence through one or more types of chemical bonds, usually through

complementary base pairing, Watson-Crick base pairing" does not clarify the metes and bounds of claims 17, 18, 20, and 23-28. It is noted that the pointed to support provides disclosure of one or more types of chemical bonds and recites "complementary base pairing, Watson-Crick base pairing" as an example; however, said support does not provide the criteria to which one of skill in the art may apply for determining a nucleic acid sequence being complementary to another sequence as specified by the elected claims.

REJECTION RE-ITERATED

8. Specific to claims 17 and 23-28, line 2, the term "complementary" causes the claim to be vague and indefinite because it is not clear what criteria are being used to determine that a nucleic acid sequence is complementary to another. Is a complement of 2 nucleotides of two different nucleotides sequence sufficient to consider said sequence complementary? Clarification of the metes and bounds is required. Claims 18 and 20 are rejected for being dependent from claim 17.

CLAIM REJECTIONS - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent

any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

11. Claims 1-3, 5, 16-18, 20, 23-50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Manduchi et al. (2000) taken with Allzadeh et al. (2000) in combination with Lockhart et al. (US 6,040,138 A).

12. This rejection is maintained with respect to claims 1-3, 5, 16-18, 20, and 23-50, as recited in the previous office action mailed December 29, 2003.

RESPONSE TO ARGUMENT

13. Applicant argues that claim 1 comprises a method for selecting a probe for a target nucleic acid molecule, and the instant claimed invention provides a process for identifying and selecting the "best probe" for a specific target nucleic acid sequence. Further, Applicant argues that Manduchi et al. does not disclose or suggest a method for determining "appropriate probes" on the basis of the probe's hybridization signal ratio to the average hybridization ratio of the other probes for the same nucleic acid sequence. Applicant's arguments have been acknowledged and found to be unpersuasive as discussed below.

14. Manduchi et al. does not disclose a method for selection of a probe on a microarray for a target nucleic acid sequence wherein two samples types (first composition and second composition) and the ratios from the two separate two-channel microarrays are compared using the same reference for one of the channels (page 685, column 2, Introduction § and

page 687, column 1, lines 1-15). For each homotypic group and for each gene tag, Manduchi et al. computes the average intensity of that tag over a plurality of samples in the group, sets the group in order, establishes a reference group to which other groups are compared, and lists the ratios (page 687, column 1, line 46-53 to column 2, lines 1-29). Up regulation is determined by comparing ratio r_i of the average intensity of a gene tag at group I and the average intensity of the same gene tag at the reference group (page 690, column 1, lines 36-40). The method of Manduchi et al. is applied to hybridizing 3 or more candidate probes (page 686, Figure 1) generating datasets containing five homotypic groups comprising human blood progenitor cells (page 691, column 2, lines 1-10). The re-iterated citation of Manduchi et al. above is consistent with the limitations of steps a) to g) of claim 1 for selecting a probe for a target nucleic acid sequence.

15. Specific to the argument that Manduchi et al. does not disclose or suggest a method for determining "the best" or "appropriate probes" on the basis of the probe's hybridization signal ratio to the average hybridization ratio of the other probes for the same nucleic acid sequence. Claim 1 recites steps a) to g) for selecting a probe for a target nucleic acid sequence; however, said claim does not recites any limitations or steps for determining "the best" or "appropriate probes". Therefore, the pointed to citation of Manduchi et al. above is consistent with the limitations of steps a) to g) for selecting a probe for a target nucleic acid sequence.

16. Specific to Applicant's argument that Allzadeh et al. and Lockhart et al. do nothing to remedy the deficiency of Manduchi et al. as directed to claim 1, Applicant's argument directed to the deficiency of Manduchi et al. has been addressed above. Further, the

combination of Manduchi et al., Allzadeh et al. and Lockhart et al. has been directed to the limitations claims 2, 30, and 32-37, which depend from claim 1.

17. Specific to Applicant's argument that the disclosure of Manduchi et al. and Allzadeh et al. are directed to disparate arts, the cited disclosures of Manduchi et al. and Allzadeh et al. clearly illustrate that said disclosures and the claimed invention due in the same art.

18. Specific to Applicant's comment (page 23, last paragraph) regarding Manduchi et al. being accepted on March 21, 2000, and published in August 2000, said comment has been noted; however, said comment does not help Applicant overcome the instant prior art rejection.

REJECTION RE-ITERATED

19. Manduchi et al. discloses a method for selection of a probe on a microarray for a target nucleic acid sequence wherein two samples types (first composition and second composition) and the ratios from the two separate two-channel microarrays are compared using the same reference for one of the channels (page 685, column 2, Introduction § and page 687, column 1, lines 1-15). For each homotypic group and for each gene tag, Manduchi et al. computes the average intensity of that tag over a plurality of samples in the group, sets the group in order, establishes a reference group to which other groups are compared, and lists the ratios (page 687, column 1, line 46-53 to column 2, lines 1-29). Up regulation is determined by comparing ratio r_i of the average intensity of a gene tag at group I and the average intensity of the same gene tag at the reference group (page 690, column 1, lines 36-40). The method of Manduchi et al. is applied to hybridizing 3 or more candidate probes (page 686, Figure 1)

generating datasets containing five homotypic groups comprising human blood progenitor cells (page 691, column 2, lines 1-10), as in instant claims 1, 3, 5, 20, 29, 31, and 40-50.

20. It is noted Manduchi et al. discloses a method directed to highly parallel gene expression experiments, such as hybridization array experiments (page 685, column 2, lines 11-14). Although Manduchi et al. demonstrates said method with data generated from a two-channel microarray, said method is applicable to many types of data generated from highly parallel hybridization array experiments (page 686, column 2, lines 23-24).

21. It is well know in the art that a type of highly parallel hybridization array experiment is oligonucleotide arrays wherein gene expression is detected by the complementary of probe sequence to target sequence. The inclusion of a reference by Lipshutz et al. is not being used as prior art but to expand on what is well known in the art of parallel hybridization array experiments. Lipshutz et al. discloses that gene expression is detected by the complementary of probe sequence to target sequence wherein said sequence complementary to at least 15 contiguous nucleotides of the target sequence (Figure 2), as in instant claims 16-18, 23, 24, 27, and 28.

22. Further, the inclusion of the Duggan et al. reference is not being used as prior art but to expand on what is well known in the art of parallel hybridization array experiments. Duggan discloses the used of cDNA microarrays wherein fluorescent tagged transcripts are, on average 600 bp, have an average of 2 fluor tags per 100 bp and hybridize, all of them (contiguous), to their probe (page 12, column 1, lines 23-26) as in instant claims 25 and 26.

23. However, Manduchi et al. (2000) does not disclose the limitations of claims 2, 30, and 32-37.

24. Allzadeh et al. discloses a method of generating said data by hybridizing select gene probes on a "lymphochip" (first partner) to labeled targets from a cDNA libraries (second partner comprises a label) (page 504, columns 1-2, Construction of a specialized DNA microarray §, Analysis of gene expression in lymphoid malignancies §, and page 510, Microarray Procedures §), as in instant claims 2 and 34-37.

25. Further, the samples for microarray analysis disclosed by Allzadeh et al. comprises a low and high concentration and samples are treated in such growth conditions as phorbol ester, ionomycin, or anthracycline (page 510, columns 1-2, Messenger RNA samples §), as in instant claims 30, 32, and 33.

26. However, Manduchi et al. and Allzadeh et al. do not disclose the limitation wherein the first or second binding partner comprises biotin.

27. Lockhart et al. discloses the use of labels such as biotin for nucleic acids (probe or target) in expression monitoring by hybridization to high-density oligonucleotide arrays (column 13, lines 62-67), as in instant claims 38 and 39.

28. Lockhart et al. suggests an improvement for monitoring gene expression via hybridization arrays by using a rapid and effective method for identifying a set of oligonucleotide probes that maximized specific hybridization efficacy (column 2, lines 18-33). The improvement suggested by Lockhart et al. is directly applicable to the method of parallel gene expression experiments via hybridization arrays (page 685, column 2, Introduction §) of Manduchi et al. via the method of Allzadeh et al. as cited by Manduchi et al.

29. An artisan of ordinary skill in the art at the time of the instant invention would have been motivated by the improvement suggested by Lockhart et al. to perform a method of parallel gene expression experiments via hybridization arrays as taught by Manduchi et al. and Allzadeh et al. using biotin as taught by Lockhart et al. Therefore, it would have been obvious to one having ordinary skill in the art at the time of the invention was made to perform method of parallel gene expression experiments via hybridization arrays with biotin as taught by Manduchi et al., Allzadeh et al., and Lockhart et al.

CONCLUSION

30. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

31. A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

32. This application contains claims 4, 6-15, 19, 21, 22, and 51-67 drawn to an invention nonelected with traverse, October 02, 2003. A complete reply to the final rejection must

include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

33. Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 193), and 1157 OG 94 (December 28, 1993) (see 37 CFR § 1.6(d)). The CM1 Fax Center number is (703) 872-9306.

34. Any inquiry concerning this communication or earlier communications from the examiner should be directed to C. Dune Ly, whose telephone number is (571) 272-0716. The examiner can normally be reached on Monday-Friday from 8 A.M. to 4 P.M.

35. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, Ph.D., can be reached on (571) 272-0722.

36. Any inquiry of a general nature or relating to the status of this application should be directed to Legal Instruments Examiner, Tina Plunkett, whose telephone number is (571) 272-0549.

C. Dune Ly
6/7/04

ARDIN H. MARSCHEL
PRIMARY EXAMINER 6/11/04